Remarks

Claims 1-13 were examined and are pending in the present application. The previous objections to the specification and enablement rejections under 35 U.S.C. §112 were withdrawn. Applicants have amended Claim 1 to incorporate the limitations of Claims 3 and 9, and cancelled Claims 3 and 9.

Rejections under 35 U.S.C. § 102(b)

Claims 1-10 and 12-13 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Aoyama et al. Claims 1-13 were rejected under 35 U.S.C. § 102(b) as anticipated by Wang. Claims 1-3 and 12-13 as amended were rejected under 35 U.S.C. § 102(b) as anticipated by Peng et al. Claims 1-13 were rejected under 35 U.S.C. § 102(b) as anticipated by Nagai et al. These rejections are respectfully traversed if applied to the amended claims.

The Claimed Subject Matter

Claim 1 as presently amended is directed to a method of preventing and/or treating asthma by administering a composition consisting essentially of a therapeutically effective dose of luteolin, wherein the luteolin is administered orally, in an amount ranging from 0.1 to 10 mg/kg of body weight.

Aoyama

Aoyama discloses that the alcoholic extract obtained from the *Perilla* seed "contains one or more compounds selected from apigenin, chrysoeriol, luteolin and rosmarinic acid" (or "resomarinic acid," according to the Derwent English Abstract). Paragraph 21 states that when the crude extract is purified, apigenin fractions have the highest activity. Aoyama appears to teach the extraction and use of a crude product, or, alternatively, the extraction and purification of apigenin, since it has the highest activity.

Other compositions that include apigenin, such as chamomile tea, are associated with a side effect (drowsiness) not observed, at least not to the same extent, with luteolin. Thus, the purified luteolin as claimed provides a benefit, in that it does not cause the similar drowsiness as that caused by crude luteolin extracts that include apigenin. Further, while disclosing that apigenin has the highest activity, Aoyama does not disclose how much luteolin would be required (as a lower activity compound) to be an effective dosage.

The claims as amended specify the optimal dosage range for luteolin, a compound which Aoyama identified as being less preferred than apigenin, and for which Aoyama did not identify an effective dosage.

Applicant therefore respectfully submits that Aoyama does not disclose what a therapeutic amount of any single compound in the disclosed extract may be, let alone what an effective amount of luteolin might be. Accordingly, Aoyama does not disclose the subject matter of the claims as amended.

Wang

Wang discloses that luteolin is effective at treating bronchitis, and the various symptoms associated with bronchitis. Bronchitis and asthma are separate indications, and only a small percentage of people with bronchitis develop asthma.

Anticipation based on inherency must rely on results that necessarily flow from the prior art. The treatment of asthma does not necessarily flow from the administration of luteolin to bronchitis patients. Accordingly, the use of luteolin to treat bronchitis is not sufficient to anticipate a claim directed to the use of luteolin to treat asthma, at all, let alone at the claimed dosage rate.

Accordingly, the rejection should be withdrawn.

Peng

Peng discloses the subcutaneous injection of luteolin into animals. The rejection over Peng was limited to Claims 1-3 and 12-13. As the limitations of (non-rejected) Claim 9 were incorporated into Claim 1, it is believed that this rejection has now been mooted.

Nagai

The Office Action states that Nagai teaches administering Sho-seiryu-to once or daily for a week to inhibit both immediate and late phase reactions in mice sensitized with anti-DNP monoclonal IgE antibodies and DNP antigen. Although Applicants believe that Nagai did not teach that Sho-seiryu-to is useful for treating asthma, only for reducing inflammation, generally, any teaching regarding Sho-seiryu-to is irrelevant to the claimed invention, which relates to using

compositions consisting essentially of luteolin, orally administered in specific dosage ranges, to treat asthma.

Nagai teaches (see page 39 of the translation) that luteolin (and other flavonoids baicalein and quercetin) **differed from Sho-seiryu-to** and Oriental-medical preparations, in that they did not show a direct antagonistic effect on histamine, serotonin, or PAF. The effects are mainly an inhibition of the release of arachidonic acid metabolites from mast cells, such as leukotriene, thromboxane, and PGD2, and inhibition of cytokine production, but not a direct antagonistic effect.

Accordingly, since Nagai teaches that the effect of luteolin and Sho-seiryu-to are different, any teaching by Nagai related to the use of Sho-seiryu-to cannot be said to anticipate, or even render obvious, the claimed invention.

The Office Action further points to Figure 29 as teaching inhibition of the "late phase," but in fact, Figure 29 is directed to a teaching of the use of luteolin on skin (cutaneous) reactions in BALB/c mice. Skin irritation is not asthma. Nagai's teachings of treating skin irritation neither anticipate nor render obvious the claimed treatment of asthma. At best, Nagai teaches that luteolin has the ability to inhibit cytokine and histamine release. The teachings regarding the inhibition of mast arachadonic metabolites from mast cells (Figure 32), or the inhibition of cytokines such as TNF-alpha or IL-6, do not teach using luteolin to treat asthma at all, let alone at the claimed dosage ranges.

It is Applicants' belief that Nagai neither anticipates, nor renders obvious, the claimed subject matter.

Rejections under 35 U.S.C. § 103 (a)

Claims 1-13 were rejected under 35 U.S.C. § 103 (a) as obvious over Nagai in view of Aoyama. Claims 1-13 were also rejected under 35 U.S.C. § 103 (a) as obvious over Aoyoma in view of Nagai or Kimata. These rejections are respectfully traversed if applied to the amended claims.

It is respectfully submitted that, in addition to the other previously discussed deficiencies in Nagai and Aoyama, neither Nagai nor Aoyoma teach an effective dose of luteolin for treating asthma. Accordingly, the combination of references fails to teach each element of the claimed invention.

Kimata teaches that luteolin inhibits mast cell activation by inhibiting calcium ion influx and PKC activation. However, Kimata does not teach that luteolin would be effective in treating asthma, let alone at the claimed dosage ranges.

The most the secondary references teach is that luteolin, at some concentration, in a cellular assay, interacts with various receptors that may be implicated in a variety of disorders, without specifically disclosing asthma as a disorder that may be treated, or specifying a dosage range for such treatment. Applicants submit that this teaching is not effective to render the claimed invention obvious.

Accordingly, it is asserted that the references, alone or in combination, do not render obvious the subject matter as presently claimed.

Conclusion

Claims 1-2, 4-8, and 10-13 as amended herein are believed allowable, and an early notice to such effect is earnestly solicited. Should the Examiner have any questions or comments regarding the foregoing Amendment, he is urged to telephone the undersigned attorney.

Respectfully submitted,

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